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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,770	03/06/2001	Todd M. Kinsella	A-68614-1/RMS/RMK	3911
24353	7590	07/14/2004	EXAMINER	
BOZICEVIC, FIELD & FRANCIS LLP 200 MIDDLEFIELD RD SUITE 200 MENLO PARK, CA 94025			WESSENDORF, TERESA D	
			ART UNIT	PAPER NUMBER
			1639	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,770	KINSELLA, TODD M.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/23/04.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59-86 is/are pending in the application.
- 4a) Of the above claim(s) 62 and 66-86 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 59-61 and 63-65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Claims

Claims 1-58 have been cancelled.

Claims 59-86 are pending.

Claims 62 and 66-86 have been withdrawn from consideration as being drawn to non-elected invention.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59-61 and 63-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons set forth in the last Office action.

Response to Arguments

Applicants argue if an element of a claim is not new, it does not have to be described in any detail, citing MPEP.

What is presently claimed is a retroviral vector encoding a fusion protein, a so called "split intein" protein, that is capable of cyclizing a polypeptide of interest (which is positioned within the fusion protein) to form a cyclic polypeptide. Applicants argue that in the background section of the instant application, split intein proteins for the production of cyclic peptides are known in the art.

In response, as correctly pointed out by applicants the claim recites a retroviral vector (i.e., a compound). How can a compound be new, if the elements are not new? A compound is not discrete but an entity or unit. Applicant's arguments as to the split intein protein being known in the art are not commensurate in scope with the claimed compound which does not explicitly recite for a split intein protein. If an applicants choose to rely upon general knowledge in the art to render his disclosure complete, applicants must show that anyone skilled in the art would have actually possessed the knowledge, In re Lange (CCPA 1981) 644 F2d 856, 209 USPQ 288. There is no explicit description in the specification as to the compound being a split intein protein as applied to claimed retroviral vector claiming not a protein but a polypeptide. The background section

in the disclosure does not recite in the context of the claimed retroviral vector a split intein. Applicants can rely upon prior art which would enable one skilled in the art to glean therefrom the necessary information to render the specification complete with respect to the first paragraph of 35 USC 112 but the burden is on applicants to point out precisely where such disclosure lies. In re Albrecht II (CCPA 1975) 185 USPQ 590.

However, not everything, which may be cited as prior art can be equated with common knowledge for the purposes of meeting the requirement of 112.

Applicants argue that as recognized by one of skill in the art and as explained on page 9, lines 8-25 of the instant specification, any synthetically-made or naturally-occurring split intein can be used in the subject methods. Naturally-occurring split inteins (e.g., the Ssp dnaE intein) and artificially split inteins were well known in the art prior to the priority date of the instant application. Further, a listing of 22 exemplary inteins suitable for use in the subject methods is found in the last paragraph of page 9 and the second paragraph of page 10. Accordingly, at least 22 inteins suitable for use in the claimed methods are explicitly recited in the specification, and many others would have been apparent to

one of skill in the art in view of what was already known at the time of filing.

In reply, applicants' arguments are not commensurate in scope with the claims. The claims are drawn to compounds not to a method. Furthermore, as stated by applicants the specification provides a list of the specific (22) inteins. And, presents generalizations as to the other inteins that would be apparent to one skilled in the art.

Applicants respectfully submit that one of skill in the art, in view of the instant specification and what was known about inteins at the time of filing, would have instantly envisioned numerous intein-based fusion proteins encompassed by the instant claims.

In response, as correctly stated by applicants there are too numerous (i.e., general) intein-based fusion proteins. But the specifics of the intein-based fusion proteins are limited to those described therein.

Applicants admit that certain factors may effect cyclization efficiency, there is no evidence that the claim recited fusion peptide cannot be used to make a vast number of cyclic polypeptides having different amino acid sequences. Further, polypeptides that may be circularized using the subject

invention are described in the instant specification, as, e.g., polypeptides having a randomized sequence (see Fig. 15A).

In response, a "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". *University of California v. Eli Lilly and Co.*, 43 USPQ 2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). See further *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003). The claims do not recite for any structure that would result in the cyclization of the compounds. Furthermore, as correctly stated by applicants the cyclization, is a probability circumstance. It is noteworthy to cite applicants' previous REMARKS at page 16 ".....cyclization efficiency may be affected by the presence or absence of a given amino acid, the size of the peptide library, etc...." Given no structure or formula of the fusion protein, it is not readily apparent how cyclization can be achieved.

[It is suggested that applicants amend the claim to the specific components of the retroviral to obviate this rejection].

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Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 59-61 and 63-65 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons advanced in the last Office action and reiterated below.

It is not clear as to whether the peptide of interest is different from the cyclic peptide. Furthermore, it is not clear as to which part of the fusion polypeptide undergoes cyclization to form a cyclic peptide.

Response to Arguments

Applicants urge that with the amendments to the claims "comprising an amino acid sequence" the rejection has been overcome. However, even with the said amendment the rejection still holds. The amendments provide for more confusion and simply repetitive. It is considered that peptide fundamentally contains amino acid sequence.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 59-61 and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scott (PNAS) or Evans et al (The Jnl. of Biol. Chem.) in view of Nolan et al (6,153,380) for reasons advanced in the last Office action.

Response to Arguments

Applicants urge that effective November 29, 1999, the Nolan reference is disqualified as prior art against the claimed invention if that subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. The invention claimed in the instant patent application was subject to an obligation of assignment to Rigel Pharmaceuticals, Inc. An assignment executed by the inventor Todd Kinsella was recorded on August 27, 2001. The Nolan patent cited as art was owned by Rigel at the time the claimed invention in that patent

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was made, as evidenced by an assignment by the inventor Gary Nolan to Rigel, recorded on October 14, 1997.

In reply, the rejection is based on 103(a) not 103(c). See MPEP 706.02(a).

Applicants acknowledge that the Nolan is prior art but submit that Nolan taken with either or both of Scott and Evans, still does not provide a suggestion to combine their teachings or a reasonable expectation to obtain the present invention. Applicants admit cyclizing methods involving split inteins, such as the ones referred to by Scott and Evans, represent a completely different method to that explicitly described by Nolan.

In reply, Nolan is employed not for the purpose of the cyclizing methods. Rather, Nolan is employed for the advantages derived in the use a retroviral instead of a bacterial vector. Scott and Evans, as admitted by applicants, are the ones that discloses cyclization of split inteins albeit, in a bacterial vector, as claimed. Applicant cannot show non-obviousness by attacking the references individually where the rejection is based on a combination of references. In re Young, 159 USPQ 725 (CCPA 1968).

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims 62 and 66-86 drawn to nonelected inventions. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw

July 9, 2004